

ART 34 AMDT

Claim - 27 -

18. An agent according to ~~any preceding Claim~~ in which the lectin has been enzymatically modified.

19. An agent according to ~~any preceding Claim~~ in which the lectin has been chemically modified.

20. An agent according to ~~any preceding Claim~~ wherein, if the heavy chain (H-chain) of a clostridial neurotoxin is present, the H_C domain of the H-chain is removed or modified.

21. An agent according to ~~any preceding claim~~ in which the H-chain, if present, is modified by chemical derivatisation to reduce or remove its native binding affinity for motor neurons.

22. An agent according to ~~any of Claims 1-20~~ in which the H-chain, if present, is modified by mutation to reduce or remove its native binding affinity for motor neurons.

23. An agent according to ~~any of Claims 1-20~~ in which the H-chain, if present, is modified by proteolysis.

24. An agent according to Claim 20 in which, if the H-chain is present, the H_C domain is completely removed leaving only the H_N-fragment of a clostridial neurotoxin.

25. An agent according to ~~any preceding Claim~~ in which the derivative of the clostridial neurotoxin, or fragment thereof, is obtained from botulinum neurotoxin.

26. An agent according to ~~any preceding Claim~~ in which the derivative of the clostridial neurotoxin, or fragment thereof, is obtained from botulinum neurotoxin type A.

27. An agent according to ~~Claims 1-25~~ in which the derivative of the clostridial neurotoxin, or fragment thereof, is obtained from botulinum neurotoxin type B.

- 28 -
Claim 1

28. An agent according to any of ~~Claims 1, 2, or 4-25~~ (except when dependent on Claim 3) which is formed by the coupling of a galactose-binding lectin to the LH_N fragment of botulinum neurotoxin type A.

- 5 29. An agent according to Claim 28 which is formed by the coupling of the galactose-binding lectin from *Erythrina cristagalli* to the LH_N fragment of botulinum neurotoxin type A.

- 10 30. An agent according to Claim 28 which is formed by the coupling of the galactose-binding lectin from *Erythrina corallodendron* to the LH_N fragment of botulinum neurotoxin type A.

- 15 31. An agent according to Claim 28 which is formed by the coupling of the galactose-binding lectin from *Glycine max* to the LH_N fragment of botulinum neurotoxin type A.

Claim 1
An agent according to ~~any preceding Claim~~ in which the H-chain, if present, is obtained from a different clostridial neurotoxin than that from which the L-chain is obtained.

- 20 32. An agent according to Claim 32 in which the H-chain is obtained from botulinum neurotoxin type A and the L-chain from botulinum neurotoxin type B.

- 25 34. An agent according to Claim 32 in which the H-chain is obtained from botulinum neurotoxin type A and the L-chain from tetanus neurotoxin.

Claim 33
An agent according to ~~Claims 33 and 34~~ in which the H-chain component is the H_N fragment of botulinum neurotoxin type A.

- 30 36. An agent according to ~~any preceding Claim~~ in which the L-chain or L-chain fragment is linked to the H-chain, if present, by a direct covalent linkage.

37. An agent according to any of ~~Claims 1-35~~ in which the L-chain or L-chain fragment is linked to the H-chain, if present, by a covalent linkage which includes one or more spacer regions.

5 38. An agent according to ~~any preceding Claim~~ in which the clostridial neurotoxin derivative incorporates polypeptides produced by recombinant technology.

10 39. An agent according to ~~any preceding Claim~~ in which the lectin is linked to the clostridial neurotoxin-derived component by a direct covalent linkage.

40. An agent according to ~~any of Claims 1-38~~ in which the lectin is linked to the clostridial neurotoxin-derived component by a covalent linkage which includes one or more spacer regions.

15 41. An agent according to ~~any preceding Claim~~ in which the lectin and clostridial neurotoxin components are produced as a recombinant fusion protein.

20 42. An agent according to ~~any preceding Claim~~ in which the lectin protein has been modified from its native polypeptide sequence whilst retaining an ability for the protein to bind to oligosaccharide structures, in which the terminal residue is derived from galactose or N-acetylgalactosamine.

25 43. An agent according to Claim 42 in which the protein modification results from modification of the nucleic acid coding for the lectin protein from its native sequence.

44. An agent according to ~~any preceding Claim~~ which prevents the release of a neurotransmitter or neuromodulator from a primary sensory afferent.

30 45. An agent according to ~~any preceding Claim~~ which inhibits the release of a neurotransmitter or neuromodulator from a primary nociceptive afferent.

46. A method for obtaining an agent according to ~~any preceding Claim~~ which comprises

the covalent attachment of a galactose-binding lectin to a derivative of a clostridial neurotoxin, in which the derivative of the clostridial neurotoxin comprises the L-chain or an L-chain fragment which includes the active proteolytic domain of the light (L) chain, linked to a molecule or domain with membrane translocating activity.

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47. A method for obtaining an agent according to ~~any of Claims 1-45~~ which comprises the covalent attachment of a galactose-binding lectin to a derivative of a clostridial neurotoxin with the inclusion of one or more spacer regions, in which the derivative of the clostridial neurotoxin comprises the L-chain or an L-chain fragment which includes the active proteolytic enzyme domain of the light (L) chain, linked to a molecule or domain with membrane translocating activity.

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48. A method according to Claim 46 or ~~47~~ in which the membrane translocation domain is derived from the heavy chain of a clostridial toxin.

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49. A method according to Claim 46 or ~~47~~ in which the membrane translocation domain is derived from a non-clostridial source.

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50. A method for obtaining an agent according to ~~any of Claims 1-45~~ which comprises constructing a genetic construct which codes for the agent, incorporating said construct into a host organism and expressing the construct to produce the agent.

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51. A method of controlling the transmission of sensory information from a primary sensory afferent to a projection neuron by applying the agent of ~~any one of Claims 1-45~~.

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52. A method of controlling the transmission of sensory information from a primary nociceptive afferent to a projection neuron by applying the agent of ~~any one of Claims 1-45~~.

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53. A method according to Claim 51 or ~~Claim 52~~ wherein the transmission is the release of a neurotransmitter or neuromodulator.

Sab 54. A method of controlling the sensation of pain by applying the agent of any one of *Claim 1*
Sab 54. Claims 1-45.

55. Use of the agent according to any one of Claims 1-45 or a pharmaceutically
5 acceptable salt thereof as a medicament for the alleviation and/or prevention of pain.

56. Use of the agent according to any one of Claims 1-45 in the manufacture of a
medicament for the alleviation and/or prevention of pain.

10 *Sab* 57. A method of alleviating and/or preventing pain which comprises administering an
Sab 57. effective dose of the agent according to any one of Claims 1-45. *Claim 1*